REMARKS

This Application has been carefully reviewed in light of the Office Action mailed May 9, 2006. At the time of the Office Action, Claims 1, 3-6, 8-14 and 17 were pending in this Application. Claims 1, 3-6, 8-14 and 17 were rejected. Claims 1, 5, 6, 11, 12 and 17 have been amended to further define various features of Applicants' invention. Claims 2, 7, 15 and 16 were previously cancelled without prejudice or disclaimer. Applicants respectfully request reconsideration and favorable action in this case.

Rejections under 35 U.S.C. § 103

Claims 1, 3-6 and 8-10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 4,900,720 issued to Ronald Kotitschke ("Kotitschke") in view of U.S. Patent No. 5,919,369 issued to Stephen R. Ash ("Ash"), U.S. Patent No. 5,661,124 issued to Stephen J. Hoffman et al. ("Hoffman") and U.S. Patent No. 4,968,432 issued to Glenn D. Antwiler ("Antwiler"). Applicants respectfully traverse and submit the cited art combinations, even if proper, which Applicants do not concede, does not render the claimed embodiments of the invention obvious.

Claims 11-14 and 17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Antwiler in view of Ash, Kotitschke and Hoffman. Applicants respectfully traverse and submit the cited art combinations, even if proper, which Applicants do not concede, does not render the claimed embodiments of the invention obvious.

In order to establish a *prima facie* case of obviousness, the references cited by the Examiner must disclose all claimed limitations. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). Furthermore, according to § 2143 of the Manual of Patent Examining Procedure, to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the

reasonable expectation of success must both be found in the prior art, not in applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Applicants note that conventional hemofilters are generally designed to avoid sieving of albumin. Replacement fluids used with conventional hemofiltration generally include only pharmaceutical grade, balanced salt solution. Applicants note that none of the references cited by the Examiner show or teach a plasma colloid replacement fluid, a plasma colloid replacement fluid kit or an extracorporeal blood circuit as defined in the amended claims.

The rejections of Claims 1, 3-6 and 8-10 were based upon the teachings of Kotitschke in combination with other references cited by the Examiner. Kotitschke discloses fluids containing immunoglobulins. For example see Kotitschke Col. 3, lines 30-47. Further Kotitschke identifies albumin and immunoglobulins IgG, IgA and IgM as part of "the most essential human serum proteins in the plasma-exchange medium." Kotitschke Col. 3, lines 29-33. Other human serum proteins are also identified in Kotitschke.

The need for immunoglobulins in Kotitschke's replacement fluid is logical because Kotitschke's goal is to provide a plasmapheresis replacement fluid. See Kotitschke Col. 1, lines 6-21. Plasmapheresis removes immunoglobulins. In contrast, very large pore hemofiltration as defined in amended Claims 1, 6, 11, 12, and 17 avoids removal of significant amounts of immunoglobulins and similar large molecules. Such hemofiltration may be performed using an effective molecular weight cutoff that does not remove immunoglobulins. As a result, at least some replacement fluids disclosed in the present application exclude immunoglobulins. Immunoglobulins need not be replaced if they are not substantially removed in the first place.

Because it focuses on plasmapheresis, Kotitschke does not teach or suggest a "plasma colloid replacement fluid" or a "source for infusing clean albumin and clean target receptor molecules," as further defined in the amended Claims. In fact, by identifying immunoglobulins as "essential" in its plasma-exchange medium, Kotitschke teaches against any replacement fluid that does not contain immunoglobins. Therefore, Kotitschke may not be combined with the other references cited by the Examiner to arrive at the presently claimed invention.

Kotitschke relates to a sterile plasma-exchange medium. Col. 1, lines 7-8. Such a medium is designed to replace a patient's plasma with a substitute medium. Col. 1, lines 9-14. As noted on page 9, lines 3-13 of the specification, Applicants' very large pore hemofiltration avoids removal of significant amounts of immunoglobulins and similar large molecules because removal of these molecules may be associated with a marked increase in the risk of opportunistic infection.

Kotitschke recognized problems with opportunistic infection when immunoglobulins are removed. See Kotitschke Col. 3, lines 20-24 of Kotitschke. For example, Kotitschke states in Col. 2, lines 1-3 "Depletion of the immunoglobulins due to plasma exchange could also increase the patient's risk of contracting infections." Kotitschke expressly teaches the use of a "serum protein solution (protein level 75g-l) in a plasma exchange." See Col. 3, line 52 -Col. 4, line 10. To prevent such infection, Kotitschke expressly teaches the use of a plasma exchange medium which includes immunoglobulins IgG, IgA and IgM. In contrast, Applicants' invention as claimed is related to very large pore hemofiltration which avoids removal of significant amounts of immunoglobulins and similar large molecules. Kotitschke clearly teaches a substantially opposite approach to minimizing infections as Applicants' claimed invention.

As Applicants' specification states "[v]ery large pore hemofilter 102 will typically have pores with a molecular weight cutoff substantially less than that of plasmapheresis filters, so that no significant amount of immunoglobulins and similar large molecules will be sieved from the blood." p. 22, lines 17-22. The specification also indicates that Applicants' plasma colloid replacement fluid includes "albumin and/or other target receptor molecules and/or other physiologic molecules in a sufficient concentration to adequately replenish ongoing losses." p. 24, lines 1-5.

Claim 1 has been amended to call for various features of Applicants' invention including, but not limited to, "A plasma colloid replacement fluid for replacing target receptor molecules ... removed from a patient's body during very large pore hemofiltration which avoids removal of significant amounts of immunoglobulins and similar large molecules...." Applicants respectfully submit that Kotitschke expressly teaches a plasma exchange medium which includes a wide variety of constituents such as immunoglobulins

IgG, IgA, and IgM other than Applicants' ". . . clean target receptor molecules including clean albumin, clean receptor molecules and clean carrier molecules . . ." as further defined in amended Claim 1.

Applicants note that Claim 1 as amended also calls for "... the clean target receptor molecules having binding sides operable to attract inflammatory mediators from tissue spaces and tissue binding sites of the patient...." The Examiner makes reference to IgG and IgA representing inflammatory mediators. As previously noted, Applicants expressly teach avoiding removal of significant amounts of immunoglobulins and similar large molecules.

Hoffman expressly teaches novel hemoglobulin compositions useful as a substitute for red blood cells and methods of preparing such red blood cells using recombinant DNA technology. Applicants respectfully submit that Hoffman does not show or teach any type of replacement fluid such as defined in amended Claim 1 to replace target receptor molecules removed from a patient's blood during very large pore hemofiltration.

There is no basis or no teaching of any reason or benefit **(even if possible)** to combine the blood substitutes of Hoffman with the plasma replacement medium defined in Kotitschke. Applicants respectfully submit that Kotitschke teaches a sterile plasma exchange medium which includes immunoglobulins to replace immunoglobulins that have been removed during a therapeutic plasmpheresis procedure which is substantially different from Applicants' claimed plasma colloid replacement fluid. Applicants request withdrawal of all rejections and allowance of Claim 1 as amended.

Claims 3, 4 and 5 as amended are dependent from Claim 1. Since Claim 1 as amended is now deemed allowable, Claims 3, 4 and 5 as amended are allowable. Applicants request withdrawal of all rejections and allowance of Claims 3, 4 and 5 as amended.

Claim 6 as amended calls for "... plasma colloid replacement fluid for replacing target receptor molecules ... removed ... during very large pore hemofiltration which avoids removal of significant amounts of immunoglobulins and similar large molecules...." As previously noted, Kotitschke expressly teaches a sterile plasma-exchange medium which includes immunoglobulins. Applicant requests withdrawal of all rejections and allowance of Claim 6 as amended.

Claim 8, 9 and 10 are dependent from Claim 6. Since Claim 6 as amended is know deemed allowable, Claims 8, 9 and 10 are allowable. Applicants request withdrawal of all rejections and allowance of Claims 8, 9 and 10 as amended.

Claims 11-14 and 17 were primarily rejected based on Antwiler in combination with other references cited by the Examiner. Applicants respectfully note that Antwiler expressly teaches the use of a dialyzer which is used to remove low density lipoproteins and very low density of lipoproteins from the plasma portion of the patient's blood with regenerating the filtered plasma and subsequently returning the regenerated plasma to a patient. See Antwiler Col. 1, lines 6-16. Applicants' attorney has not found any use of the terms "hemofiltration" or "hemofilters" in Antwiler.

Claim 11 as amended calls for various features of Applicants' invention including, but not limited to, "... a plasma colloid replacement fluid kit ... other clean target receptor molecules disposed in the replacement fluid operable to bind target molecules thereto for removal during very large pore hemofiltration which avoids removal of significant amounts of immunoglobulins and similar large molecules ... the clean target receptor molecules operable to attract inflammatory mediators from tissue spaces and tissue binding sites of the patient." Antwiler does not show or teach any use of a **"fluid kit"** as defined in amended Claim 11. Antwiler does not show or teach plasma colloid replacement fluid having clean target receptor molecules as further defined in amended Claim 11.

Ash expressly teaches the use of a sorbent suspension with plasma filtration or hemofiltration in connection with a dialyzer. See for example Col. 11, lines 50-65. Ash further teaches the use of sorbent suspension to remove toxins when "... the plasma fraction of the blood caused to alternatively exit and re-enter the interior of the membrane." Ash Col. 2, lines 41-61. Ash does not show or teach using a replacement fluid in combination with hemofiltration as defined in amended Claim 11. For example, Ash expressly states "in the preferred dialysis system ... only molecules of about 3,000 Daltons or less will pass through the membrane." See Col. 10, lines 4-11. Applicants respectfully submit that there is no teaching to combine hemofiltration and plasmafiltration devices such as shown in Ash with Antwiler or any of the other references cited by the Examiner to reject amended Claim 11.

Applicants request withdrawal of all rejections and allowance of Claim 11 as amended.

Claim 12 has been further amended to call for various features of Applicants' invention which are neither shown nor taught by Antwiler and the other references cited by the Examiner including, but not limited to, "an extracorporeal blood circuit ... a blood filter ... the blood filter operable to form a filtered blood stream which does not contain significant amounts of immunoglobulins and similar large molecules ...." Applicants respectfully submit that Antwiler clearly teaches away from a extra corporeal blood circuit having a blood filter as defined in amended Claim 12. For example Antwiler does not include any references to albumin, the removal of albumin or the replacement of albumin. Antwiler expressly teaches "flowing the fluid past one side of a semipermeable membrane, flowing a solution containing a precipitation agent, the dialyzate, past the other side of the membrane so as to cause the precipitation agent to transfer through the membrane into the biological fluid, and precipitating the constituent from the fluid." See Antwiler Col. 1, lines 19-29. Antwiler clearly does not show or teach a blood filter forming an ultrafiltrate stream containing the target molecules and target complex molecules as defined in amended Claim 12.

Claim 12 as amended also calls for a "blood filter" and various features including, but not limited to "... the effective molecular weight cutoff selected to avoid removal of significant amounts of immunoglobulin to prevent increasing the risk of opportunistic infection ... a source for infusing clean albumin and clean target receptor molecules into the filtered blood stream." Neither Antwiler nor any of the other references show or teach the combination of features of Applicants' invention as defined in amended Claim 12.

Applicants request withdrawal of all rejections and allowance of Claim 12 as amended.

Claims 13 and 14 are dependent from Claim 12. Since Claim 12 as amended is now deemed allowable, Claims 13 and 14 are allowable.

Applicants respectfully submit that the references cited by the Examiner do not show or teach an extracorporeal blood circuit having an effective molecular weight cut-off as defined in amended Claim 12 in combination with an effective molecular weight cut-off less

than approximately one million Daltons (Claim 13) or on effective molecular weight cut-off less than approximately five hundred thousand Daltons (Claim 14). Applicants respectfully request withdrawal of all rejections and allowance of Claims 13 and 14.

Claim 17 has been further amended to call for various features of Applicants invention including, but not limited to, "an extracorporeal blood circuit ... a blood filter ... the blood filter and other portions of the circuit operable to remove an ultrafiltrate from the portion of a patient's blood supply with ultrafiltration rates between approximately two liters per hour and twenty liters per hour ... the effective molecular weight cut-off of the blood filter selected to avoid removal of significant amounts of immunoglobulins and similar large molecules ... the clean target receptor molecules in the replacement fluid replacing the target molecules and the target complex molecules sieve from the portion of the patient's blood by the blood filter ... the replacement fluid providing sufficient albumin to maintain adequate plasma oncotic pressure with ultrafiltration rates between approximately two liters per hour and twenty liters per hour." Neither Antwiler nor Ash show or teach an extracorporeal blood circuit for hemofiltration as defined in amended Claim 17. Applicants request withdrawal of all rejections and allowance of Claim 17 as amended.

Petition For Extension Of Time

Applicants respectfully submit herewith a Petition for Two-Month Extension of Time Request. Applicant authorizes the Commissioner to charge the amount of $225.00 for the required filing fee.

CONCLUSION

Applicants have now made an earnest effort to place this case in condition for allowance in light of the amendments and remarks set forth above. Applicants respectfully request reconsideration of the pending Claims as amended.

Applicants believe a fee as required under 37 C.F.R. §1.17(a)(2) is due with this response in connection with the request for a two-month extension of time. This fee is included with this response. Applicant authorizes the Commissioner to charge the amount of $225.00 for the Request for Extension of Time. Applicants believe there are no additional fees due at this time, however, the Commissioner is hereby authorized to charge any fees necessary or credit any overpayment to Deposit Account No. 50-2148 of Baker Botts L.L.P.

If there are any matters concerning this Application that may be cleared up in a telephone conversation, please contact Applicants' attorney at 512.322.2599.

Respectfully submitted,
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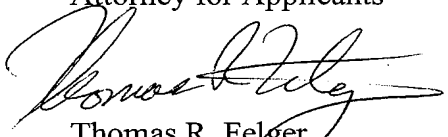

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Enclosures: Petition for Two Month Extension of Time